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15-Year Follow-up of Neuromuscular Function in Patients With Unilateral Nonreconstructed Anterior Cruciate Ligament Injury Initially Treated With Rehabilitation and Activity Modification: A Longitudinal Prospective Study.

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1 **15-year Follow-up of Neuromuscular Function in Individuals with**
2 **Unilateral Non-reconstructed ACL Injury Initially Treated with**
3 **Rehabilitation and Activity Modification: A Longitudinal**
4 **Prospective Study**

5

6 ***Running title: 15-year Follow-up of Neuromuscular Function after ACL Injury***

7

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17

1 **Abstract**

2 **Background:** It has been suggested that neuromuscular function is of importance in the
3 overall outcome after ACL injury.

4 **Hypothesis:** Good neuromuscular function can be achieved and maintained over time in
5 subjects with ACL injury, treated with rehabilitation and activity modification, but without
6 reconstructive surgery.

7 **Study Design:** Case series

8 **Methods:** One hundred consecutive patients (42 women and 58 men) with acute ACL injury
9 at a non-professional, recreational or competitive, activity level were assessed 1, 3 and 15
10 years after injury. Their mean age at inclusion was 26 years (range 15 to 43). All patients
11 initially underwent rehabilitation and were advised to modify their activity level, especially
12 by avoiding contact sports. Patients with recurrent giving-way episodes and/or secondary
13 meniscus injuries that required fixation, were subsequently excluded and underwent
14 reconstruction of the ACL. Sixty-seven patients (71%) with unilateral non-reconstructed
15 injury remained at the 15-year follow-up. Fifty-six of these 67 patients were examined with
16 the one-leg hop test for distance and knee muscle strength. The Limb Symmetry Index (LSI),
17 i.e., dividing the result for the injured leg by that of the uninjured leg and multiplying by 100,
18 was used for comparisons over time (paired t-test).

19 **Results:** The LSI for the one-leg hop test was higher at the 3-year (mean 98.5%, SD 7.6%)
20 than at the 15-year follow-up (mean 94.8%, SD 10.5%) (mean difference -3.7%, 95% CI -
21 6.1% to -1.2%, P=0.004). The LSI for isometric extension was higher at the 15-year (mean
22 97.2%, SD 13.7%) than at the 1-year follow-up (mean 88.2%, SD 15.4%) (mean difference
23 9.0%, 95% CI 3.7% to 14.4%, P=0.001). At the 15-year follow-up, between 69% and 85% of
24 the patients had an LSI \geq 90%.

1 **Conclusions:** Good functional performance and knee muscle strength can be achieved and
2 maintained over time in the majority of patients with ACL injury treated with rehabilitation
3 and early activity modification, but without reconstructive surgery.

4

5 **Key Terms:** Anterior cruciate ligament, rehabilitation, neuromuscular function, follow-up
6 studies

7

1 INTRODUCTION

2 ACL injuries are common with a yearly incidence of 0.81 per 1000 inhabitants aged 10 to 64
3 years¹³. Rehabilitation is normally included in the treatment after injury or reconstruction of
4 the ACL²⁷. Despite the fact that surgical treatment is widely used, there is still no evidence as
5 to whether surgical or non-surgical treatment is best for these patients²⁰. It is, however, well
6 known that the risk of future joint problems, in the form of functional limitations, secondary
7 lesions, and osteoarthritis (OA), is increased following such an injury^{11,29}.

8

9 Neuromuscular function is the complex interaction between sensory and motor pathways.
10 Defective neuromuscular function, leading to reduced strength and functional performance,
11 alterations in movement and muscle activation patterns, proprioceptive deficiencies, and
12 impaired postural control, is commonly seen after an ACL injury¹. Improvements in
13 neuromuscular function can be achieved by appropriate rehabilitation^{19,27}. It has been
14 suggested that neuromuscular function is of importance for the overall outcome after ACL
15 injury¹⁰, and that long-term follow-up studies are needed in order to establish the role of
16 neuromuscular function in future joint problems after knee injury²⁹. However, to our
17 knowledge, there are few prospective, longitudinal, long-term follow-up studies on patients
18 with ACL injury, treated with or without reconstructive surgery, where measures of
19 neuromuscular function are included^{22,32}. Only one of these studies reports comparisons over
20 time³².

21

22 The aim of the present study was to evaluate functional performance and knee muscle
23 strength at 15 years compared with 1 and 3 years after the initial injury in subjects with
24 unilateral non-reconstructed ACL injury. Forty-two women and 58 men (mean age 26 years,
25 range 15 to 43) at a non-professional, recreational or competitive, activity level (i.e., patients

1 on a professional athletic level were excluded) were included in the study 15 years ago. The
2 patients were initially treated with rehabilitation and advice regarding activity modification.
3 Those with recurrent giving-way and/or secondary meniscus injuries that required fixation,
4 were subsequently excluded from the study and underwent reconstruction of the ACL⁴⁰. At
5 the 15-year follow-up, 67 subjects (71%) still had a unilateral non-reconstructed ACL injury,
6 and the majority of these individuals had a good knee function and an acceptable activity
7 level¹⁸. In the present study, we hypothesized that good functional performance and knee
8 muscle strength could be achieved and maintained over time in the majority of the subjects
9 with unilateral non-reconstructed ACL injury.

10

11 **SUBJECTS AND METHODS**

12 **Patients**

13 Between the years 1985 and 1989, 200 patients presenting with an acute knee sprain
14 combined with hemarthrosis and/or instability at manual testing were referred, within 5 days,
15 by the emergency unit at the █████ University Hospital for further evaluation by the same
16 orthopedic surgeon (████) specializing in knee injuries. Patients presenting at times when this
17 physician was off-duty (n=100) were not included in the study. Inclusion criteria when the
18 patients entered the study 15 years ago were: 1) age between 15 and 45 years, 2) acute knee
19 trauma to a previously normal knee, with complete ACL rupture, with or without associated
20 lesions of other structures of the knee, and 3) an uninjured contralateral extremity. Patients on
21 a professional athletic level (i.e., a Tegner score of 10) and not willing to accept a decrease in
22 activity level (n<5), those who specifically requested a primary ligament reconstruction (n=2–
23 3), those with fracture seen on radiographs, or those with psycho-social disorders were
24 excluded. The patients' mean age at inclusion was 26 years (range 15 to 43). The cause of
25 injury was ball sports (n=59), alpine skiing (n=30), and other activities (n=11)⁴³. The

1 diagnosis was verified in all patients by stability testing and arthroscopy, by the same
2 orthopedic surgeon (■■■■), within ten days of injury. Meniscal tears were not sutured at the
3 time of this study. Resections were made on menisci with large, unstable lesions whereas
4 smaller or partial tears were left untreated. Collateral ligament lesions were not operated on,
5 and the ACL was not reinserted or reconstructed. A detailed description of the patients' knee
6 injuries (e.g. number of patients with isolated ACL injury, and associated lesions) has been
7 provided in other reports^{18, 40, 43}.

8
9 The patient cohort comprising 100 consecutive patients was followed prospectively at regular
10 intervals for three years^{2, 12, 40, 42, 43}. These 100 patients were contacted for a long-term
11 follow-up assessment at a mean of 15 years after the initial injury (SD 1.4 years). Six of these
12 patients were lost to follow-up (four had moved abroad and two did not reply). Sixty-seven
13 subjects (71%) still had a unilateral non-reconstructed ACL injury, 22 (23%) subjects had
14 undergone ACL reconstruction, and 6 (6%) had sustained an ACL injury to the contralateral
15 knee (one of these patients had also undergone reconstructive surgery). The number of
16 patients from initial injury to the 15-year follow-up has been described in detail elsewhere¹⁸.
17 Fifty-six (20 women and 36 men) of the 67 subjects with unilateral non-reconstructed ACL
18 injury at the 15-year follow-up attended the assessment of neuromuscular function (Figure 1).
19 Five of these 56 subjects (1 woman and 4 men) had radiographic tibiofemoral OA, and 19 (5
20 women and 14 men) had suffered a major meniscal tear (which had been sutured or resected).
21 The subjects' age, height, weight, and Knee injury and Osteoarthritis Outcome Score (KOOS)
22^{30, 31} at the 15-year follow-up are given in Table 1. Their Tegner activity level³⁶ and Lysholm
23 knee score³⁶ at the time of injury (Tegner activity level), and at 1, 3, and 15 years after the
24 injury are given in Table 2. Details on activity level and subjective function have been given
25 elsewhere¹⁸. The reported decrease in activity level in the long-term perspective (from 6 to 4)

1 may reflect a normal adaptation to older age and changed phase of life¹⁸. This decrease is
2 comparable to that of a control group of uninjured subjects⁴.

3

4 Eleven subjects (7 women, 4 men) did not attend the assessment of neuromuscular function
5 due to the following reasons: six subjects had moved from the region, three declined to
6 participate, and two subjects were not able to perform the test due to pregnancy (n=1) or a
7 recently sustained hamstring rupture (n=1). These subjects did not differ from those who
8 attended the assessment of neuromuscular function with regard to age (P=0.17), activity level
9 (P=0.16), Lysholm score (P=0.29) or KOOS (P=0.32 – 0.98).

10

11 The Research Ethics Committee of █████ University approved the study. All subjects gave
12 their written informed consent to participate in the study.

13

14 **Treatment algorithm**

15 The aim of the initial treatment was to achieve good knee function without discomfort or lack
16 of confidence in the knee, on a satisfactory activity level from the patient's perspective. The
17 aim was also to reduce the risk of new injuries and degenerative changes in the longer
18 perspective. The treatment algorithm included: 1) non-operative treatment, 2) rehabilitation,
19 3) advice regarding activity modification, and 4) ACL reconstruction in selected cases;
20 because of giving way, unacceptable activity level, or re-injury resulting in a symptomatic
21 reparable meniscal tear.

22

23 *Non-operative treatment*

24 The intention was to treat the patients without primary reconstructive surgery. Patients in
25 doubt were actively encouraged not to undergo primary ACL reconstruction.

1

2 *Rehabilitation*

3 All patients underwent training; randomized to either neuromuscular training supervised by
4 physical therapists specializing in knee injury training, or self-monitored training⁴³. The
5 overall aim of both training methods was to regain joint mobility and restore muscle function.
6 The patients were allowed to use crutches as long as necessary because of pain and
7 dysfunction. They were told not to force movements if they caused pain so that the injured
8 knee structures would have time to heal. They were also asked to do exercises daily at home
9 to improve joint mobility and functional stability. The patients were told to contact the
10 physician treating them whenever necessary.

11

12 *The neuromuscular training method*, based on biomechanical and neuromuscular principles,
13 aims to improve neuromuscular control and achieve compensatory functional stability⁴⁴.
14 Physical therapists specializing in knee injury training were in charge of the training sessions.
15 All patients were given information about the function of the ACL, symptoms associated with
16 the injury, the role of the muscles in knee joint stabilization, and advice on how to avoid
17 giving way. Training started within a week of arthroscopy and continued for 5 to 8 months.
18 During the first period after injury, active movements in synergies of all the joints in the
19 injured extremity²⁶ were included to improve the mobility of the injured knee. The
20 movements started with the uninjured extremity, initiating the normal movement and applying
21 bilateral transfer effect of motor learning to the injured leg^{9,17}. To improve functional
22 stability, movements were performed in closed kinetic chains^{21,24} in different positions (e.g.,
23 lying, sitting, standing), to obtain low, evenly distributed articular surface pressure^{5,33} by
24 muscular co-activation⁵. The model emphasized the enhancement of antigravity postural
25 functions of weight-bearing muscles, and the provocation of postural reactions in the injured

1 leg by using voluntary movements in the other lower extremity, trunk, and arms^{7,9}. The goal
2 was to achieve equilibrium of loaded segments in static and dynamic situations without
3 undesirable compensatory movements, with the aim of acquiring postural control in situations
4 resembling conditions of daily life and more strenuous activities. The level of training,
5 progression, and recommended physical activity was guided by the patient's neuromuscular
6 function and not by time after injury. Strength coordination, balance, and proprioception were
7 all included in the movements. To achieve the desired requirement of postural activity, the
8 patients performed the exercises on sloping boards, to obtain axial loading of joints by
9 muscular co-activation. Progression was provided by varying the angles of the sloping board
10 in relation to the gravity line, by varying the number, direction, and velocity of the voluntary
11 movements, and also by training more complex functions, cardiovascular endurance, and
12 sports-specific skills. Training ceased when muscular postural reactions, provoked by
13 voluntary movements, were clinically evaluated as occurring without delay and were the same
14 as those on the uninjured side (based on visual inspection and palpation)⁴⁰. Examples of
15 exercises in this training method have been described by Zätterström et al.⁴⁴.

16

17 The patients in the *self-monitored training* group were given oral and written instructions by
18 physical therapists at the time of the initial arthroscopic evaluation. The intention regarding
19 this group was to resemble the natural course so far as possible, based on the assumption that
20 patients were able to carry out training on their own without supervision or continuous
21 guidance. Training consisted of traditional exercises (at the time of inclusion in this study) for
22 joint mobility and knee muscles to regain range of motion and muscle strength. Movements
23 were performed in non-weight-bearing positions, training isolated muscles in the injured leg
24 selectively, e.g., knee extensions and straight leg raises. The patients were instructed and
25 encouraged to continue the exercises for up to 12 months⁴⁰. At the six-week follow-up, 49%

1 of these patients were transferred to the neuromuscular supervised training group because of
2 restricted joint mobility and/or considerable muscle atrophy⁴⁰. Consequently, the majority of
3 the patients underwent neuromuscular supervised training.

4 5 *Activity modification*

6 Depending on the perceived instability, the patients were advised to modify their physical
7 activities in order to cope with the ACL insufficiency. All patients were advised to avoid
8 contact sports, particularly soccer, basketball and team handball.

9 10 *ACL reconstruction*

11 Patients with more than one significant re-injury, who would not accept a further prophylactic
12 decrease in activity level, or those with a symptomatic reparable meniscal tear, were advised
13 to undergo ACL reconstruction (n=22). Reconstructed patients were subsequently excluded,
14 since the treatment model without reconstruction had not succeeded, i.e., these patients were
15 regarded as treatment failures^{18, 40}.

16 17 **Assessment**

18 *One-leg hop test for distance*

19 We used a modified version of the one-leg hop test³⁵, with the arms free, aiming at a more
20 functional execution of the hop, thus making it easier to balance the body⁴⁰. The subjects
21 were told to hop as far as possible, taking off and landing on the same foot. The test was
22 performed three times with each leg, alternating the right and left leg, the hop distance being
23 measured from toe to toe. A trial one-leg hop preceded the measurements. The subjects wore
24 shoes, e.g., sneakers. The best value of the three hops was used in the analysis. The reliability

1 of this test is high in non-injured subjects (ICC 0.96)³, (ICC 0.92)²⁵ and in individuals with
2 ACL injury (ICC 0.89)²⁵.

3

4 *Knee muscle strength*

5 Measurements of isometric and concentric isokinetic strength of the knee muscles, used and
6 described previously in this patient group⁴⁰, were performed with a Biodex Multi-Joint
7 System II isokinetic dynamometer (Biodex Medical Systems Inc., Shirley, New York, NY,
8 USA) with Biodex Advantage software, version 4.5. The Biodex dynamometer has been
9 shown to be reliable (ICCs > 0.90) and valid^{34,37}. The standard Biodex knee unit attachment
10 was used. Subjects were placed in an upright position with 90° hip flexion on the Biodex
11 dynamometer chair, and were secured with straps across the chest, pelvis, thigh and ankle.
12 The resistance pad was placed as distally as possible on the tibia while still allowing full
13 dorsiflexion at the ankle. The center of motion of the lever arm was aligned as accurately as
14 possible with the slightly changing flexion-extension axis of the knee joint. The subjects
15 gripped the edge of the chair in order to stabilize the body during the test. Standardized verbal
16 instructions and encouragement were given. The subjects were allowed trial tests in order to
17 familiarize themselves with the equipment and the test procedure. Measurements of isometric
18 muscle strength were followed by isokinetic muscle strength testing. *Isometric muscle*
19 *strength test:* With the knee in 60° flexion, three maximum isometric contractions of the knee
20 extensors and flexors were performed. The contraction time and relaxation time were both 5
21 seconds. Peak torque (Nm) was used in the analysis. *Isokinetic muscle strength test:* The
22 isokinetic concentric knee muscle strength was measured by 40 consecutive maximal
23 reciprocal contractions at an angular velocity of 90°·s⁻¹. The range of motion of the knee joint
24 was defined as 0 to 100°. Peak torque and total work (Nm or J) were used in the analysis.

25

1 **Statistical analysis**

2 Since factors other than the knee injury may affect muscle strength and hop distance over a
3 period of several years, such as age and/or a decrease in activity level, comparisons of
4 absolute values were deemed not to be appropriate. Moreover, the Cybex II device, which
5 was used at the 1- and 3-year follow-ups⁴⁰, was no longer available at the 15-year follow-up.
6 The fact that different isokinetic devices were used at the follow-ups also makes comparisons
7 of absolute values over time inappropriate. Therefore, to reduce the effect of confounding
8 factors in the analysis, the Limb Symmetry Index (LSI), i.e., dividing the result for the injured
9 leg by that of the uninjured leg and multiplying by 100, was used for comparisons over time.
10 An LSI greater than or equal to 90% for an individual was considered normal^{8,23}.

11
12 The primary comparison over time was between the 1- and the 15-year follow-ups, since
13 active training may be needed up to 1 year (or less) after the injury^{28,40}, and since it has been
14 suggested that the maximum capacity of knee function is reached about 1 year after
15 injury/reconstruction and training¹⁰. However, improvements in neuromuscular function have
16 been observed up to 18 months or more after injury^{16,28,39,41}. For this reason, we also
17 analyzed the LSI between the 3- and the 15-year follow-up, to elucidate whether
18 improvements at median term follow-up were maintained at long-term follow-up. The
19 primary outcome was the LSI for the one-leg hop test, where a 5% difference was considered
20 clinically relevant. A sample size calculation estimated that at least 38 patients would be
21 required to show a 5% difference in LSI between the 1- and the 15-year follow-up for the one-
22 leg hop test (SD_{diff} 11.0) with 80% power at the 5% significance level.

23
24 No differences were observed in LSI values between men and women or between the training
25 groups (according to the initial randomization, i.e., intention-to-treat). There were too few

1 patients with OA (n=5) to permit comparisons of LSI values between those with and without
2 OA. Subgroup analysis was performed regarding LSI values at the 15-year follow-up in
3 patients with and without major meniscal tear.

4

5 The paired t-test was used for the intra-group comparisons, and the independent t-test for the
6 inter-group comparisons. A level of $P \leq 0.05$ was chosen to indicate statistical significance.

7

8 **RESULTS**

9 **One-leg hop test for distance**

10 Mean (SD), LSI, and mean differences (95% CI) between follow-ups are given in Table 3.

11 Mean LSI values at the follow-ups were greater than 94%. The LSI was higher at the 3-year
12 follow-up than at the 15-year follow-up ($P=0.004$) (Table 3). The number of subjects with
13 normal LSI, i.e., $\geq 90\%$, was 40 (77%) at the 1-year follow-up, 46 (89%) at the 3-year follow-
14 up, and 44 (85%) at the 15-year follow-up (Figure 2). No differences were observed between
15 the patients with and without meniscal tear at the 15-year follow-up.

16

17 **Knee muscle strength**

18 Mean (SD), LSI, and mean differences (95% CI) between follow-ups are also given in Table
19 3. Mean LSI values for the various measurements ranged from 88.2% (SD 15.4%) to 100.6%
20 (SD 30.8%) at the 1-year follow-up, from 94.6% (SD 20.6%) to 103.0% (SD 25.6%) at the 3-
21 year follow-up, and from 96.5% (SD 15.9%) to 102.2% (SD 14.3%) at the 15-year follow-up.
22 Five LSI values were over 100%; these were all observed in measurements of knee flexor
23 strength (Table 3). The LSI of peak torque isometric extension was higher at the 15-year
24 follow-up than at the 1-year follow-up ($P=0.001$) (Table 3). The number of subjects with
25 normal LSI generally increased over time (Table 4, Figure 3). The percent of subjects with

1 normal LSI for the various measurements ranged from 42% to 56% at the 1-year follow-up,
2 from 54% to 68% at the 3-year follow-up, and from 69% to 82% at the 15-year follow-up
3 (Table 4). No differences were noted between the patients with and without meniscal tear at
4 the 15-year follow-up.

5

6 **DISCUSSION**

7 In this prospective longitudinal study, 100 consecutive patients with ACL injury at a non-
8 professional, recreational or competitive, activity level were followed for 15 years. The
9 primary intention was to treat all individuals with rehabilitation, without ACL reconstruction.
10 They were also advised to modify their activities in order to cope with their injury. We
11 hypothesized that with our treatment regimen, the long-term follow-up would reveal: i) a
12 unilateral non-reconstructed ACL injury in the majority of the patients; ii) good objective and
13 subjective knee function and acceptable activity level in the patients with unilateral non-
14 reconstructed ACL injury, and iii) low prevalence of knee OA in this patient cohort. Good
15 subjective knee function and acceptable activity level¹⁸, as well as low prevalence of knee
16 OA (16%; P. Neuman, unpublished data, personal communication) have been reported in
17 these patients at the 15-year follow-up. The main finding of the present study was that good
18 functional performance and knee muscle strength were maintained over the 15-year follow-up
19 in the majority of the patients with unilateral non-reconstructed ACL injury.

20

21 Regarding the primary outcome, the one-leg hop test, high mean LSI values (i.e., a small
22 difference in hop distance between the legs) were found at all follow-ups. The LSI was
23 statistically significantly higher at the 3-year follow-up than at the 15-year follow-up (Table
24 3), which may be interpreted as a decrease in functional performance over time. However, the
25 difference was 3.7%, whereas the pre-defined clinically relevant difference was set at 5%.

1 Thus, the clinical relevance of this difference can be questioned. In line with our study,
2 Myklebust et al.²² reported a small difference between the injured and uninjured legs in the
3 one-leg hop test at a long-term follow-up (mean 9.4 years after injury, range 7 to 11 years) of
4 team handball players with and without ACL reconstruction. We found that more than 77% of
5 the patients had a normal LSI, i.e., greater than or equal to 90% (Figure 2), at the follow-ups.
6 At the 15-year follow-up, only 15% of the patients showed abnormal LSI values in the one-
7 leg hop test. Salmon et al.³² followed 97 patients with ACL reconstruction over 13 years. At
8 7 and 13 years after surgery, 93% and 66% of the patients, respectively, had normal LSI in the
9 one-leg hop test. Contrary to our results, these authors found a significant deterioration in the
10 one-leg hop test over time³².

11
12 Mean LSI values ranged from 88.2% to 98.6% for the knee extensor muscle strength
13 variables, and from 94.5% to 103.0% for the knee flexor muscle strength variables at the
14 follow-ups. The lower LSI values for the knee extensors than for the knee flexors probably
15 reflect the difficulty in restoring quadriceps muscle strength after an ACL injury²⁷. The LSI
16 for peak torque isometric extension was statistically significantly higher at the 15-year than at
17 the 1-year follow-up (Table 3). The difference in LSI was 9% (95% CI 3.7% to 14.4%),
18 which was considered a clinically relevant difference. This result indicates that improvements
19 in muscle strength can be achieved after more than one year, which also has been reported by
20 others^{28,39}. At the 1-year follow-up, about half of the subjects had normal LSI values for knee
21 muscle strength, at the 3-year follow-up more than 50% had normal LSI values, and finally at
22 the 15-year follow-up about 75% of the subjects showed normal LSI values (Table 4). This
23 result reflects improvements in limb symmetry over time in knee muscle strength. The LSI
24 values at the 15-year follow-up are higher than the side-to-side differences in knee muscle
25 strength (total work at 60°·s⁻¹ and 240°·s⁻¹) reported in team handball players about 9 years

1 after injury²², indicating better results in our study. However, since different muscle strength
2 variables were used in these studies, the results are not completely comparable.

3

4 The results of high mean LSI values at the follow-ups, the majority of the patients showing
5 normal LSI, and no deterioration in LSI over time, show that good functional performance,
6 measured by the one-leg hop test for distance, and good knee muscle strength can be achieved
7 and maintained over time. From the results of the present study, and previous results from the
8 same patient cohort^{40,41}, we conclude that good neuromuscular function can be achieved in
9 the majority of patients with ACL injury, with neuromuscular rehabilitation and activity
10 modification, without recourse to reconstructive surgery. Since elite athletes (Tegner level 10)
11 and those unwilling to accept a decrease in activity level were excluded from this study, we
12 determine whether that conclusion could be applied to those groups of individuals.

13

14 No differences were observed in LSI of the one-leg hop test or knee muscle strength in the
15 subgroup analysis of meniscal tear vs. no meniscal tear. However, previous studies have
16 shown reduced quadriceps muscle strength in patients with meniscal injury^{6,15}. Further
17 studies in a larger group of patients are needed to elucidate the short- and long-term effects of
18 meniscal injury on neuromuscular function. More research is also needed on the role of
19 neuromuscular function in future joint problems, such as OA, after knee injury²⁹.

20

21 At the 15-year follow-up, only 6 patients were lost to follow-up, yielding a 94% return.
22 Seventy-one percent of the subjects had a unilateral non-reconstructed ACL injury, 23% had
23 undergone ACL reconstruction, and 6% had bilateral ACL injuries. Patients undergoing ACL
24 reconstruction were considered as treatment failures and were subsequently excluded. A
25 limitation of our study is that we cannot analyze the effect of surgical intervention in this

1 patient cohort. Randomized controlled trials are needed in order to establish the role of
2 reconstructive surgery in the overall outcome after ACL injury. Such a study is now ongoing
3 ¹⁴. Sixty-seven patients (71%) with non-reconstructed unilateral ACL injury remained at the
4 15-year follow-up, and 56 (84%) of these were assessed regarding neuromuscular function.
5 However, the eleven patients that did not attend the assessment of neuromuscular function did
6 not differ from those who attended the assessment, with regard to individual factors or
7 subjective function. Thus, the 56 patients appear to be a representative sample of the patients
8 with unilateral non-reconstructed ACL injury.

9
10 Another limitation of this study is that no control group of uninjured subjects was included
11 initially and followed prospectively. It has been reported that neuromuscular function is
12 affected in both legs after a unilateral ACL injury ^{2,38}. Thus, high LSI values may reflect poor
13 performance in both legs. Therefore, a subject for further study is to compare the patients in
14 the present study with uninjured controls in a cross-sectional design at the 15-year follow-up.

15 16 **CONCLUSIONS**

17 Good functional performance, measured by the one-leg hop test for distance, and good knee
18 muscle strength can be achieved and maintained over time in the majority of the subjects with
19 unilateral non-reconstructed ACL injury with initial treatment consisting of neuromuscular
20 rehabilitation and activity modification.

21

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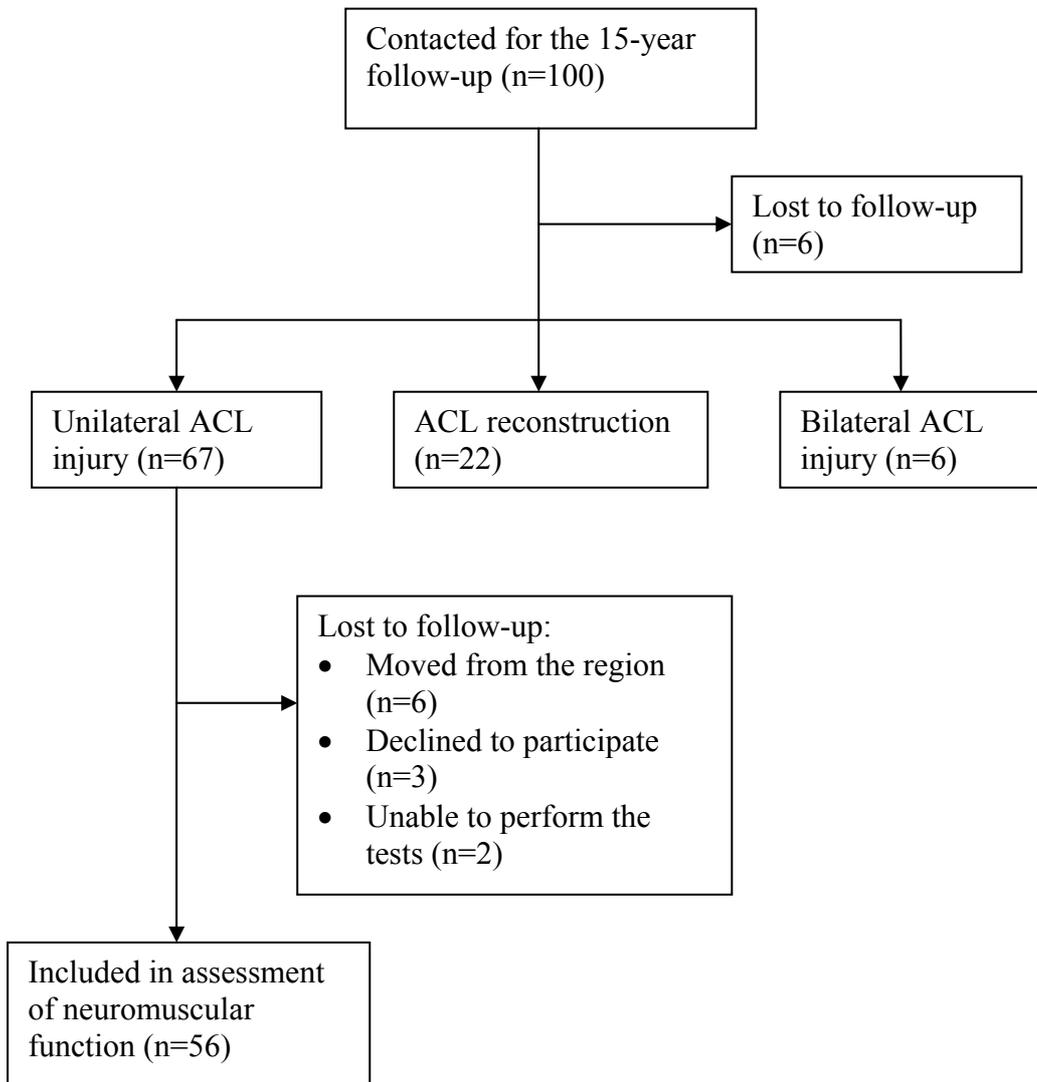
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1 **FIGURES**

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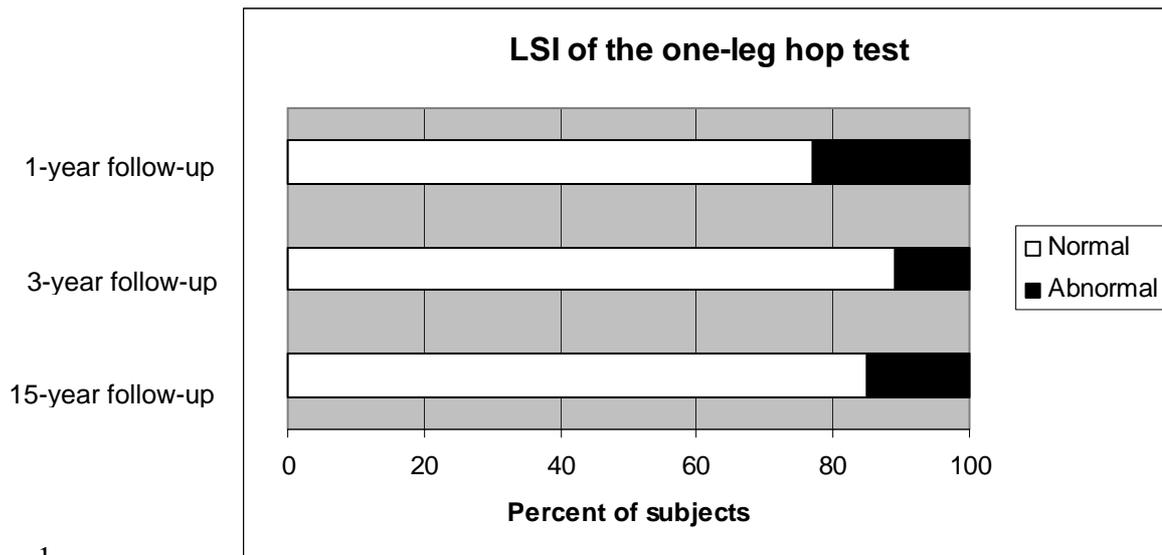
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5 **Figure 1.** Flow of participants at the 15-year follow-up.

6 *Note:* One of the subjects with bilateral ACL injury had also undergone ACL reconstruction.

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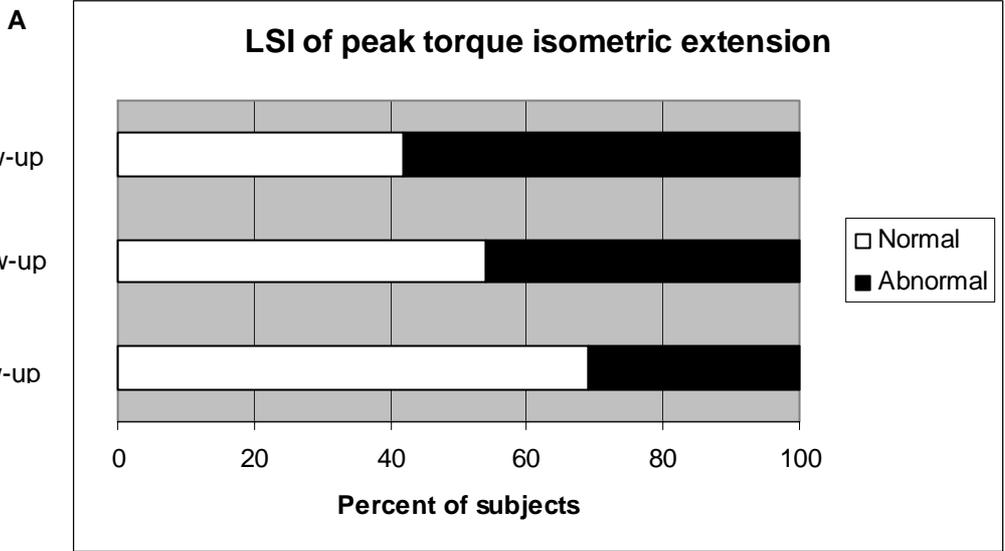


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2 **Figure 2.** Percent of subjects with normal LSI ($\geq 90\%$) and abnormal LSI ($< 90\%$) in the one-

3 leg hop test at the follow-ups.

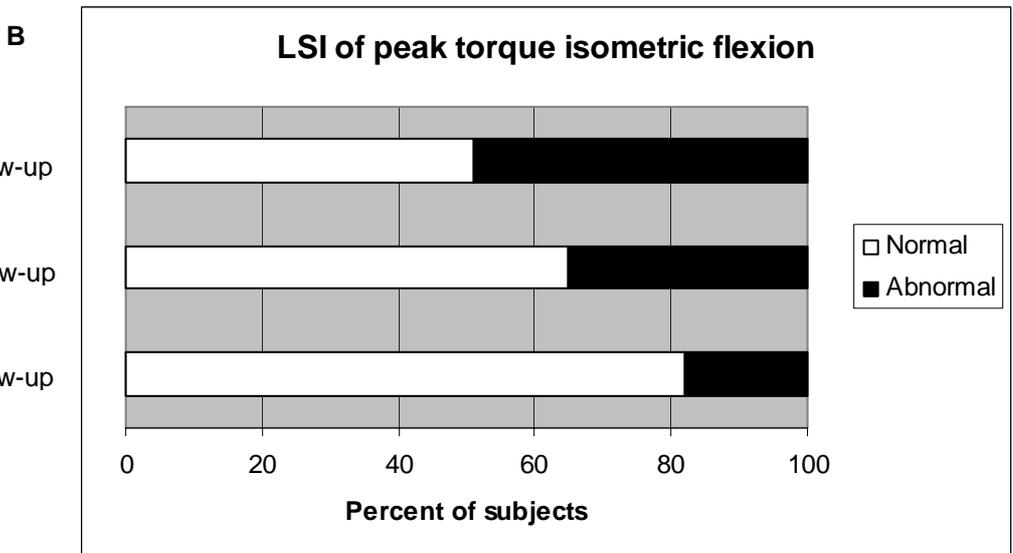
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7 **Figure 3.** Percent of subjects with normal LSI ($\geq 90\%$) and abnormal LSI ($< 90\%$) in peak
 8 torque isometric extension (A) and flexion (B) at the follow-ups.

9

TABLES

Table 1. Characteristics of the patients at the 15-year follow-up.

Characteristics	Women (n=20)	Men (n=36)	Total group (n=56)
	Mean (SD)	Mean (SD)	Mean (SD)
Age (years)	41 (7)	44 (7)	43 (8)
Height (cm)	168 (7)	181 (6)	177 (9)
Weight (kg)	73 (14)	89 (17)	83 (18)
KOOS subscales	Mean (SD), 95%CI	Mean (SD), 95%CI	Mean (SD), 95%CI
<i>Pain</i>	88 (16), 80.1–95.7	93 (12), 88.4–96.6	91 (14), 87.3–94.6
<i>Symptoms</i>	88 (14), 80.8–94.2	89 (16), 83.2–94.0	88 (15), 84.1–92.3
<i>ADL</i>	92 (12), 86.3–98.0	97 (9), 93.5–99.5	95 (10), 92.2–97.8
<i>Sport/Rec</i>	73 (29), 59.3–86.2	79 (24), 71.3–87.4	77 (26), 70.1–83.8
<i>QOL</i>	73 (27), 60.1–85.5	77 (23), 69.7–85.2	76 (24), 69.3–82.3

Table 2. Tegner activity level and Lysholm knee score at the time of injury (Tegner activity level), and at 1, 3, and 15 years after the injury.

	Women (n=20)	Men (n=36)	Total group (n=56)
Tegner activity level			
Preinjury	6 (4–7)	7 (6–7)	7 (6–7)
1 year	5 (4–6)	6 (5–7)	6 (5–7)
3 years	6 (5–6)	6 (5–7)	6 (5–7)
15 years	3 (2–4)	4 (3–5)	4 (2–5)
Lysholm knee score			
1 year	96 (6)	96 (4)	96 (5)
3 years	95 (8)	96 (8)	96 (8)
15 years	83 (19)	87 (15)	86 (17)

Median (quartiles) is given for Tegner activity level scale. Mean (SD) is given for Lysholm score.

Table 3. Mean (SD) for the one-leg hop test, isometric (peak torque) and isokinetic (peak torque and total work) knee muscle strength (extension, flexion) in the injured (inj) and uninjured (uninj) legs and Limb Symmetry Index (LSI) in percent (%) at the 1-, 3-, and 15-year follow-ups, and mean difference (95% CI) between the 1- and 15-year follow-ups and the 3- and 15-year follow-ups.

	1-year follow-up			3-year follow-up			15-year follow-up			Mean difference (95% CI)	
	Inj leg Mean (SD)	Uninj leg Mean (SD)	LSI Mean (SD)	Inj leg Mean (SD)	Uninj leg Mean (SD)	LSI Mean (SD)	Inj leg Mean (SD)	Uninj leg Mean (SD)	LSI Mean (SD)	1- vs. 15-year follow-up	3- vs. 15-year follow-up
One-leg hop test (cm) N=52*	180.8 (39.8)	188.2 (35.1)	95.7 (9.1)	185.6 (39.6)	187.9 (35.0)	98.5 (7.6)	158.2 (36.0)	166.9 (34.0)	94.8 (10.5)	-0.9 (-4.0–2.2)	-3.7 (-6.1– -1.2)
Peak torque isometric ext (Nm) N=52†	159.8 (69.7)	181.6 (73.4)	88.2 (15.4)	174.8 (73.2)	189.5 (80.4)	94.6 (20.6)	239.3 (64.1)	248.4 (64.5)	97.2 (13.7)	9.0 (3.7–14.4)	2.6 (-4.4–9.7)
Peak torque isometric flex (Nm) N=51†	81.9 (32.2)	85.4 (33.1)	100.6 (30.8)	85.4 (37.3)	88.9 (37.9)	97.6 (20.2)	113.9 (30.9)	112.9 (32.9)	102.2 (14.3)	1.6 (-8.3–11.5)	4.6 (-2.5–11.6)
Peak torque isokinetic ext (Nm) N=49†	74.9 (18.7)	81.6 (22.8)	94.1 (16.3)	80.7 (24.5)	83.5 (22.9)	97.9 (19.0)	163.9 (51.9)	171.4 (49.0)	96.5 (15.9)	2.4 (-4.1–8.9)	-1.4 (-8.4–5.7)
Peak torque isokinetic flex (Nm) N=48†	49.3 (19.0)	54.3 (22.6)	95.1 (26.3)	57.7 (21.9)	57.8 (22.3)	103.0 (25.6)	76.1 (24.2)	75.5 (24.5)	101.7 (13.9)	6.6 (-2.4–15.5)	-1.3 (-10.2–7.6)
Total work isokinetic ext (J) N=48†	3178.9 (788.9)	3451.5 (969.6)	94.5 (17.0)	3425.6 (1034.0)	3525.9 (961.9)	98.2 (18.5)	4400.7 (1167.8)	4475.7 (1082.8)	98.6 (13.7)	4.1 (-1.7–9.8)	0.4 (-6.0–6.9)
Total work isokinetic flex (J) N=47†	2078.6 (806.1)	2296.6 (944.3)	94.5 (26.0)	2440.5 (918.9)	2450.3 (929.8)	102.6 (25.8)	2067.9 (672.0)	2057.9 (661.6)	101.8 (19.8)	7.3 (-2.3–16.9)	-0.8 (-9.9–8.2)

* Patients attending all follow-ups are included in the analysis over time. Missing cases are those that did not attend the 1- or 3-year follow-up.

† Patients attending all follow-ups are included in the analysis over time. Missing cases are those that did not attend the 1- or 3-year follow-up or due to equipment problems on the test occasion.

Table 4. Number of subjects (percent) with normal LSI ($\geq 90\%$) and abnormal LSI ($< 90\%$) in the knee muscle strength variables at the follow-ups.

	1-year follow-up	3-year follow-up	15-year follow-up
	Normal LSI/abnormal LSI n (%)	Normal LSI/abnormal LSI n (%)	Normal LSI/abnormal LSI n (%)
Peak torque, isometric ext (Nm)	22/30 (42/58)	28/24 (54/46)	36/16 (69/31)
Peak torque, isometric flex (Nm)	26/25 (51/49)	33/18 (65/35)	42/9 (82/18)
Peak torque, isokinetic ext (Nm)	27/22 (55/45)	32/17 (65/35)	35/14 (71/29)
Peak torque, isokinetic flex (Nm)	27/21 (56/44)	31/17 (65/35)	38/10 (79/21)
Total work, isokinetic ext (J)	27/21 (56/44)	32/16 (67/33)	37/11 (77/23)
Total work, isokinetic flex (J)	25/22 (53/47)	32/15 (68/32)	35/12 (74/26)